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14. ABSTRACT

Surgery for breast cancer includes removal of the breast tumor along with axillarylymph nodes. Unfortunately, a relatively common side effect following axillary lymph node dissection (ALND) is upper-extremity lymphedema. The purpose of this study is to identify risk factors for lymphedema among women with breast cancer surgery. A case-control study was conducted with 94 cases with lymphedema and 94 controls that were frequency matched on type of axillary surgery and surgery date. On multivariate analysis, lymphedema cases were more likely to have active cancer status at their last follow-up, and to have received chemotherapy than controls. Greater Body Mass Index was associated with moderate or severe lymphedema. The severity of arm or hand swelling was significantly related to how much the lymphedema interfered with patients' daily activities. Quality of life was affected by lymphedema with lymphedema patients reporting significantly lower scores on the physical component scale of the SF-36.

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I. Introduction

Lymphedema is a common problem for patients diagnosed with breast cancer, with an estimated 6 – 35% developing it sometime after breast cancer treatment.[1-20] In 2007, it is estimated that 178,480 women will be diagnosed with breast cancer, and 88% of these women will survive at least 5 years.[21] The reported incidence of lymphedema varies with the length of follow-up, the measurement techniques, and other patient and treatment-related factors.[22-24] It can range from mild to severe, and can be a chronic condition that affects patients' quality of life for years after cancer surgery.[25-30] Patients are interested in learning how to prevent lymphedema because it is one of the more feared side effects following completion of treatment.

A less invasive procedure, sentinel lymph node dissection (SLND), has shown a reduction in reported lymphedema and other arm symptoms.[14, 31-40] In a study conducted at Park Nicollet Institute, 4.7% of SLND patients reported arm swelling at six months after surgery versus 19.5% of ALND patients ($p < .001$).[39] However, patients are not eligible for SLND if they have clinically positive nodes, a pathologically positive sentinel node, or if the surgeon is unable to locate the sentinel lymph node.

Several treatment-related factors have been associated with lymphedema including the extent of axillary dissection, axillary radiation therapy after surgery, type of surgery, and the presence of infection in the ipsilateral arm.[4-7,17, 41-46] Several patient-related factors have also been evaluated for their association with lymphedema in breast cancer patients including body mass index, weight training/resistance exercises, level of hand use, airline travel, hypertension, weight loss, diabetes, smoking and age at breast cancer diagnosis, and findings have been inconsistent for these factors.[1,5-7,17,19,20,44,47-53]

Previous studies have several limitations. Most of the studies have a small sample size without a comparison group, making it difficult to determine which factors are significantly associated with lymphedema. The surgery and treatments for breast cancer have changed in recent years, with a higher proportion of patients now having lumpectomy, sentinel lymph node dissection, and adjuvant treatment. Women are advised to avoid weight training/resistance exercises, constrictive pressure, and activities that could lead to arm injury or infection, but most of this advice is based on very limited or anecdotal data. Therefore, there is a need for additional studies to identify factors that contribute to the development of lymphedema in breast cancer patients.

II. Body

Specific aims. The primary specific aim of this study was to identify risk factors for lymphedema among women who have had axillary surgery for breast cancer. Secondary aims were: 1) to evaluate which factors predict moderate/severe lymphedema in patients who have lymphedema, 2) to describe patients' rating of the interference with daily life caused by lymphedema, 3) to compare the reported quality of life using the SF-36 (Short Form-36) for patients with and without lymphedema, 4) to compare arm circumference measurements to patient-reported lymphedema, and 5) to identify the cause(s) to which patients attribute their lymphedema.

Study design. This study used a matched case-control design, which permitted identification of risk factors that were present more often in lymphedema cases than in controls who had breast cancer surgery but did not developed lymphedema. Lymphedema cases were identified at the time they presented to the physical therapy department or cancer center at five participating institutions in Minnesota. The protocol and consent forms for the study were reviewed and approved by the participating Institutional Review Boards and the Department of Defense HSRRB.

Research subjects. Eligibility criteria for cases included: a clinical diagnosis of lymphedema, unilateral axillary surgery for invasive breast cancer, no known recurrent disease present in the axilla, and ability and willingness to give consent. Control participants were identified using the oncology registry. Eligibility criteria for controls included: no upper extremity lymphedema, unilateral axillary surgery for invasive breast cancer, no known recurrent disease in the axilla, and ability and willingness to give consent. Controls were matched to cases on date of axillary surgery and type of axillary dissection (sentinel versus axillary lymph node dissection). Controls were not matched on age or other factors because matching on a variable precludes the possibility of assessing its role as a potential risk factor. The final sample size was 94 cases and 94 matched controls.

Questionnaires. The Measure of Arm Symptom Survey (MASS-Version 3) was administered to cases and controls as a subjective measure of lymphedema. Breast cancer patients with lymphedema (i.e., cases) were asked to complete a revised questionnaire (MASS – Version 3 lymphedema) with questions referencing the date of the onset of arm swelling. Potential lymphedema risk factors were assessed in the MASS including diabetes, hypertension, smoking, past shoulder injury, flexibility exercises, strength training exercises, medical procedures, arm/hand injury, airline travel, body mass index (BMI) and occupation. The questionnaires address the severity of symptoms by having patients rate them on a 5-point Likert-type scale from no swelling to very severe swelling. The degree of interference with life activities was assessed using a similar 5-point scale of "not at all" to "very much." The MOS 36-Item Short-Form Health Survey (SF-36) was administered to cases and controls to assess general health-related quality of life. This questionnaire uses two summary component scales (physical and mental), and higher scores reflect greater quality of life. To assess test-retest reliability, a second MASS questionnaire was mailed to the first 24 cases in the study within two weeks after the initial questionnaires were completed. After reliability information was collected on the first 24 cases, the questionnaires were administered on a one-time basis. Arm measurements were conducted for lympedema patients using a tape measure starting at the hand and wrist, and then measuring every 4 cm along the arms. The sum of these circumferences was added and the percent differences between the treated and untreated sides were calculated.

Setting. Patients were recruited from five clinics in Minneapolis, Minnesota. Park Nicollet Health Services (PNHS) is a large multi-specialty clinic with approximately 370 breast cancer cases diagnosed annually. Fairview-University Medical Center (F-UMC) is a National Cancer Institute-designated Comprehensive Cancer Center with approximately

150 breast cancer cases diagnosed annually. Fairview Southdale Medical Center (FSMC) is a regional hospital with approximately 300 breast cancer cases diagnosed annually. The Humphrey Cancer Institute (HCI) is affiliated with North Memorial Medical Center, a regional hospital with approximately 320 breast cancer cases diagnosed annually. HealthEast Care System includes St. John's Hospital and St. Joseph's Hospital in St. Paul, Minnesota with approximately 280 breast cancer cases diagnosed annually. It was added as a recruitment site at the end of 2005 to increase enrollment. Adequate numbers of control patients are available because of the large number of breast cancer patients diagnosed annually.

Data analysis. Test-retest reliability on the MASS was assessed using Pearson correlations for continuous variables and Spearman correlations for ordinal variables. Univariate analysis was conducted to describe the characteristics of cases and controls. Matched case-control analysis using conditional logistic regression compared cases and controls on potential risk factors for lymphedema in both univariate and covariate analyses. Age, BMI, tumor size, number of nodes removed, number of positive nodes, number of aspirations were treated as continuous variables. Variables that were significant ($p<.05$) in univariate analysis were included in a multivariate analysis with stepwise selection. SAS (SAS/STAT User's Guide, version 6, 1990; SAS Institute, Cary, NC) was used for all analyses. Statistical tests and corresponding P values were two-sided.

Results

MASS reliability. Test-retest reliability correlations ranged from 0.43 to 1.0. All correlations were statistically significant. Items with a test-retest correlation less than 0.60 were excluded from further analyses. These included the following: "Since surgery, has there been a specific event that you think caused your arm or hand to swell?" (yes/no). "Since breast surgery, but before you had arm swelling, how often did you have a breast, chest or arm infection on the side of your surgery?" "Since breast surgery, but before you had arm swelling, did you wear constrictive clothing or jewelry (such as tight elastic around your wrist) on the side of your surgery?" "Since breast surgery, but before you had arm swelling, did you wear an underwire bra?" "Since breast surgery, but before you had arm swelling, how often did you participate in flexibility exercises using upper body (such as stretching or yoga)?" "Since breast surgery, but before you had arm swelling, how often did you participate in aerobic exercises (such as jogging, brisk walking, biking)?" "Since breast surgery, but before you had arm swelling, how often did you participate in vigorous repeated arm motion activities (such as bowling, golfing, painting, and wallpapering)?"

Matching variables. Cases and controls were matched on type of axillary dissection; six matched pairs underwent SLND, and 86 underwent ALND. We also attempted to match cases and controls on time since surgery within 3 months. For 75 cases we obtained a control whose surgery was within this window, and for another 17 cases we obtained a control whose surgery was within one year of that case. For the remaining 2 cases, whose surgeries took place more than a decade ago, it was necessary to relax the

temporal limit even more. Overall, the difference in date of surgery for each case and matched control averaged less than 1 month.

Disease and Treatment Factors. Cases and controls did not differ significantly in tumor size or number of axillary nodes removed (See Table 1). Cases and controls did not differ in side of surgery (dominant versus nondominant side), or receipt (yes versus no) of the following: reconstructive surgery (either type included), reconstruction using breast implant, reconstruction using TRAM procedure, radiation therapy (any location included), radiation to the breast, radiation to the supraclavicular area, or hormone therapy. They did not differ in having had drainage tubes left in place after surgery. There were, however, several disease and treatment factors that distinguished cases from controls. Cases were significantly more likely to have undergone mastectomy rather than lumpectomy (p=.008), radiation to the axilla (p=.011), and chemotherapy (p=.033). Although cases and controls did not differ significantly in nodal status (positive versus negative), the number of positive nodes was significantly higher in cases than controls (p=.009). Cases were significantly more likely to have had fluid aspirated from the axilla following breast surgery (p=.012), and the number of such aspirations were significantly higher in cases than controls (p=.005).

Demographic and Clinical Factors. Cases and controls did not differ significantly in current age, age at time of surgery, personal history of diabetes or hypertension, handedness, smoking history (ever/never), or having a prior medical condition limiting their hand or shoulder movement. BMI was significantly higher in cases than controls (p=.019).

Post-treatment factors. The MASS included questions about the occurrence of several events or activities following breast surgery. Cases and controls did not differ in reporting an injury of the arm or hand on the side of surgery, or medical procedures (e.g., blood drawn, IV administration, blood pressure taken) on the side of surgery. Cases and controls did not differ in whether they wore a breast prosthesis or whether they wore a compression sleeve to prevent arm swelling. Cases were more likely than controls to report that they participated in routine activities that caused aching of the arm on the side of surgery (such as carrying a purse, typing on a computer) (p=.019). Two additional factors demonstrated protective effects: Cases were less likely than controls to report strength training exercises using the upper body (such as weight-lifting and curl-ups) (p=.014), and they were less likely than controls to report air travel (p=.0005).

Although no participants had metastatic disease at time of diagnosis, a query of the oncology registry showed that several participants had experienced recurrent disease. Cases were significantly more likely than controls to have evidence of cancer at the time of last contact (p=.008).

Multivariate analyses. Based on these univariate analyses showing that mastectomy, number of positive nodes, radiation to the axilla, chemotherapy, BMI, number of aspirations of the axilla, doing routine activities causing arm aching, strength training, air travel, and cancer status (evidence of cancer at the time of last contact) were significant

predictors of lymphedema, all these factors were entered in a multivariate analysis with stepwise selection. The resulting model retained three factors: cancer status (OR=13.01, p=.003), air travel (OR=0.22, p=.006), and chemotherapy (OR=4.23, p=.047).

Predictors of moderate/severe lymphedema. Additional analyses were restricted to the 45 cases who indicated on the MASS that their arm or hand swelling was moderate, severe, or very severe (see Table 2). Conditional logistic regression analyses compared these cases and their matched controls. Even though the sample size for these analyses was reduced nearly by half, the following factors continued to be significant: Cases were more likely to have received radiation to the axilla (p=.037), to have had more aspirations from the axilla (p=.045), to have a higher BMI than controls (p=.01), were less likely than controls to report strength training exercises (p=.032), and were more likely to have evidence of cancer at the time of last contact (p=.038) . In addition, two factors that were not significant in analyses comparing all cases and controls emerged as significant predictors of moderate, severe, or very severe swelling: Cases were more likely to have smoked (ever versus never) (p=.004), and were more likely to have had breast surgery on their nondominant side (p=.048). When all of these factors were entered in a multivariate analysis with stepwise selection, the model retained one factor: Cases with moderate, severe or very severe swelling had higher BMI (OR=1.27, p=.011).

Lymphedema Interference with Daily Life. Of the lymphedema cases, 45 patients (49%) reported mild arm or hand swelling, 29 patients (32%) reported moderate arm or hand swelling, and 16 patients (17%) reported severe or very severe arm or hand swelling. The severity of arm or hand swelling was significantly related to how much it interfered with patients' daily activities (see Figure 1).

Quality of Life using SF-36 Health Assessment. The SF-36 scores were significantly higher (indicating better health) for controls versus cases in the subscales of physical function, role function attributed to physical problems, bodily pain, general health, vigor, social function, role limitations due to emotional problems, but not significantly different between the two groups in mental health scores The physical component summary scale was significantly higher for controls than cases, but the mental component summary scale was not significantly different between the two groups (See Figure 2).

Arm measurements. The mean percent difference in the sum of arm circumference of the affected and unaffected arm of cases was 9.0 (standard deviation (SD)=8.0, median=7.4). The mean percent difference was 6.5, 9.6, and 16.9 for cases who on the patient-reported questionnaire indicated they had mild, moderate, or severe swelling, respectively. All of the controls indicated they had no swelling.

Attribution by Lymphedema Patients. Patients were asked the "Since surgery, has there been a specific event that you think caused your arm or hand to swell?" Fifty-two cases (55%) provided a positive response to the question listing an event that they thought caused swelling. The most common things listed were recreational activities, trauma/infection to the arm or hand, and lifting heavy weight (See Table 3).

Summary of Results. On multivariate analysis, two factors were associated with lymphedema: those patients with active cancer status at the last contact, and those patients who received chemotherapy. One factor was associated with not having lymphedema (more likely among cases than controls): air travel. When evaluating predictors of moderate, severe, or very severe lymphedema (45 matched pairs), only one factor predicted lymphedema on multivariate analysis: a higher BMI.

Patients reported greater interference with daily life caused by lymphedema depending on the severity of lymphedema. SF-36 scores also reflected a decrease in quality of life (except in the mental health component) that was associated with lymphedema.

Patients-reported severity of lymphedema correlated well with arm measurement. Although over half of the lymphedema patients were able to identify an event which caused their lymphedema, many of the "causes" identified were not validated by the composite data. The most common causes identified included recreational activities, trauma/infection to the arm or hand, and lifting heavy weights.

III. Key Research Accomplishments

A list of key research accomplishments reported according to the categories on the Statement of Work are reported below:

- Preparation to begin the study (9/2003 – 8/2004)
  - Determined staff and roles on the study
  - Reviewed and revised MASS instrument with input from the lymphedema education group
  - Presented protocol and consent forms to 3 local IRBs (Fairview IRB is used for both Fairview University and Fairview Southdale sites; Park Nicollet Institute IRB for the Community Oncology Programs is used for Park Nicollet Health Services and HealthEast Care Systems) and obtained IRB approval to begin enrollment
  - Received approval from the USAMRMC HSRRB to enroll research subjects
  - Developed database and data dictionary for the study

- Accrual and data collection (12/2003 – 8/2007)
  - A total of 94 lymphedema cases were enrolled in the study
  - Matched controls were identified for the lymphedema cases and surveys were mailed to potential controls. If surveys were not returned by the controls, a subsequent control was identified and sent a survey. This was continued until surveys were received from a matched control (n=94) for each case.
  - Arm measurements were taken for each case by either the physical therapist at the time of lymphedema consult (prior to any lymphedema therapy) or at the time the prevalence case was identified in the oncology clinic.
  - Demographics, and disease and treatment-related data was collected from the medical records on all participants and recorded on the patient intake sheet.

- Progress reports and amendments were submitted to the local IRBs and annual approval was granted from the local IRBs and the USAMRMC HSRRB to continue enrollment of research subjects at the 5 institutions.

- Data entry (12/2003 – 8/2007)
  - All data was entered into Excel as cases and controls were enrolled

- Data analysis (9/2004 – 9/2007)
  - Univariate analysis was conducted to describe the characteristics of cases and controls.
  - Matched case-control analysis using conditional logistic regression compared cases and controls on potential risk factors for lymphedema in both univariate and covariate analyses. Variables that were significant ($p<.05$) in univariate analysis were included in a multivariate analysis with stepwise selection.
  - SAS (SAS/STAT User's Guide, version 6, 1990; SAS Institute, Cary, NC) was used for all analyses.

IV. Reportable Outcomes

- Research training of the principal investigator – Karen Swenson, RN, PhD, AOCN earned a PhD in Nursing from the University of Minnesota, May 2006.
- Poster presentation P20-15 entitled "Predictors of lymphedema following breast cancer surgery" was presented on preliminary data from this study at the Era of Hope Department of Defense Breast Cancer Research Program Meeting, June 8 – 11, 2005.
- Manuscript in progress entitled "Case-control study to evaluate predictors of lymphedema after breast cancer surgery" to be submitted for publication November 2007 in the *Journal of Clinical Oncology*.
- Manuscript in progress entitled "The impact of lymphedema on quality of life outcomes in breast cancer patients" to be submitted for publication November 2007 in the *Clinical Journal of Oncology Nursing.*

V. Conclusions

This case control study found that cancer status (having active cancer on the most recent follow-up or undergoing treatment for recurrent disease) was the most important predictor of lymphedema. Receipt of chemotherapy was also found to be associated with lymphedema. Although patients were excluded from the study if they had a known recurrence to the axilla, lymphedema cases may have been more likely to have active disease in the breast, chest wall, and regional lymph nodes that contributed to lymphedema. Air travel was found to be "protective" against lymphedema – this factor is puzzling and more detailed analysis will be done to determine if air travel was a "proxy" for overall general health status (identified on the SF-36), or if patients who were undergoing additional treatments with radiation or chemotherapy for metastatic disease were less likely to engage in air travel. This study provides additional evidence that age at

breast cancer diagnosis and activities of daily living such as lifting, minor arm/hand injuries, strength training and air travel do not contribute to lympedema.

When evaluating moderate/severe/very severe lymphedema, BMI was the only significant predictor of lymphedema on multivariate analysis. Other prospective and case control studies have found that BMI was a significant predictor of lymphedema,[27, 51, 53] and a recent clinical trial found that weight loss may significantly reduce lymphedema.[52] Other factors may have been important for predicting more severe lymphedema, but the number of patients with moderate or severe lymphedema may have limited the power to detect differences in this study. Further study is needed to determine if other factors that were significant on the univariate analysis such as number of aspirations after surgery, axillary radiation, and smoking status are predictive, and strength training is protective for moderate or severe lymphedema.

Limitations to this study are the inclusion of prevalence as well as incidence cases of lymphedema. Although this allowed us to nearly reach our projected sample size, it may have been more difficult for lymphedema cases to sort out which factors may have occurred prior to the development of their lymphedema. Lymphedema cases were more likely to have active cancer at their last follow-up which impacted their subsequent treatment and overall general health status.

Finally, lymphedema affects quality of life including physical problems, bodily pain, general health, vigor, social function, and role limitations. The severity of arm or hand swelling in this study was significantly related to how much lymphedema interfered with patients' daily activities. This indicates that lymphedema is an important chronic side effect that impacts women's quality of life.

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Table 1. Results of Univariate Conditional Regression Analyses.

	Cases (n=94)	Controls (n=94)	OR	P value
Type of Axillary Dissection[a]			1.0	1.0
SLND	8 (8.5)	8 (8.5)		
ALND	86 (91.5)	86 (91.5)		
Years since surgery[b]				
Median	3.8	3.9	1.58	.264
Mean	6.1	6.1		
SD	5.1	4.8		
Range	0.5 - 29.3	0.7 – 25.9		
Current age, years				
Median	57.5	60.0	.997	.833
Mean	58.4	59.5		
SD	12.0	11.9		
Range	31 – 92	34 - 86		
Type of surgery			2.18	.008
Mastectomy	71 (75.5)	51 (54.3)		
Lumpectomy	23 (24.5)	43 (45.7)		
Side of surgery			.667	.160
Right	40 (42.5)	50 (53.2)		
Left	54 (57.5)	44 (46.8)		
Side of surgery			.643	.144
Dominant	41 (43.6)	51 (54.3)		
Nondominant	53 (56.4)	43 (45.7)		
Reconstructive surgery			0.81	.517
Yes	22 (23.7)	26 (27.7)		
No	71 (76.3)	68 (72.3)		
Implant surgery			.765	.466
Yes	16 (17.2)	20 (21.3)		
No	77 (82.8)	74 (79.6)		
TRAM surgery			1.00	1.00
Yes	6 (6.5)	6 (6.4)		
No	87 (93.5)	88 (93.6)		
Number of nodes removed			1.01	.657
Median	16	15.5		
Mean	15.2	15.0		
SD	8.0	7.6		
Range	1 – 38	1 – 46		
Number of positive nodes			1.136	.009
Median	2.0	1.0		
Mean	3.9	1.9		
SD	5.6	2.5		
Range	0 – 38	0 – 11		

Table 1. (Cont.)

Nodal status			1.636	.198
Positive	65 (75.6)	61 (64.9)		
Negative	21 (24.4)	33 (35.1)		
Tumor size, mm			1.178	.102
Median	2.5	2.0		
Mean	3.0	2.3		
SD	2.1	1.5		
Range	0.0 – 10.0	0.0 – 9.0		
Radiation Therapy			1.05	.876
Yes	64 (68.8)	64 (68.1)		
No	29 (31.2)	30 (31.9)		
Radiation to breast			.833	.547
Yes	59 (63.4)	64 (68.1)		
No	34 (36.6)	30 (31.9)		
Radiation to axilla			3.60	.011
Yes	21 (22.6)	8 (8.5)		
No	72 (77.4)	86 (91.5)		
Radiation to supraclavicular area			1.21	.591
Yes	26 (28.0)	23 (24.5)		
No	67 (72.0)	72 (76.6)		
Chemotherapy			2.33	.033
Yes	77 (83.7)	65 (69.1)		
No	15 (16.3)	29 (30.8)		
Hormone therapy			.542	.075
Yes	58 (62.4)	70 (74.5)		
No	35 (37.6)	24 (25.5)		
BMI			1.059	.019
Median	27.4	25.0		
Mean	29.1	26.5		
SD	7.4	5.9		
Range	18.3 – 62.8	17.9 – 50.3		
Diabetes			1.091	.835
Yes	14 (14.9)	13 (13.8)		
No	80 (85.1)	81 (86.2)		
Hypertension			.905	.752
Yes	30 (31.9)	32 (34.0)		
No	64 (68.1)	62 (66.0)		
Drainage tubes			1.444	.396
Yes	80 (87.0)	77 (82.8)		
No	12 (13.0)	16 (17.2)		

Table 1. (Cont.)

Number of aspirations (continuous)			1.884	.005
None	66 (72.5)	81 (87.1)		
One	6 (6.6)	7 (7.5)		
Two	8 (8.8)	2 (2.1)		
Three	3 (3.3)	3 (3.2)		
More than three	8 (8.8)	0		
Prior medical condition limiting hand or shoulder movement			1.80	.292
Yes	9 (9.8)	5 (5.4)		
No	83 (90.2)	87 (94.6)		
Medical procedure on arm or hand on side of surgery			0.94	.862
Yes	24 (26.4)	25 (26.9)		
No	67 (73.6)	68 (73.1)		
Injury on arm or hand on side of surgery			0.61	.280
Yes	10 (10.9)	15 (16.3)		
No	82 (89.1)	77 (83.7)		
Strength training exercises			0.36	.014
Frequently/ very frequently	11 (11.8)	26 (28.3)		
Never/occasionally	82 (88.2)	66 (71.7)		
Routine activities causing arm to ache			2.25	.019
Frequently/ very frequently	33 (35.1)	17 (18.9)		
Never/occasionally	61 (64.9)	73 (81.1)		
Whirlpool, hot tub, or sauna use			0.50	.258
Frequently/ very frequently	4 (4.3)	8 (8.7)		
Never/occasionally	89 (95.7)	84 (91.3)		
Usually lift more than 10 pounds			0.64	.144
Yes	37 (41.1)	47 (52.2)		
No	53 (58.9)	43 (47.8)		
Any air travel since breast surgery			0.23	.0005
Yes	46 (49.5)	69 (74.2)		
No	47 (50.5)	24 (25.8)		

Table 1. (Cont.)

Wears breast prosthesis			1.38	.371
Yes	34 (36.2)	29 (30.8)		
No	60 (63.8)	65 (69.1)		
Ever wear compression sleeve			0.80	.638
Yes	12 (12.8)	14 (14.9)		
No	82 (87.2)	80 (85.1)		
Smoking			1.21	.493
Ever	40 (42.6)	35 (37.2)		
Never	54 (57.4)	59 (62.8)		
Age at time of surgery			0.99	.794
Median	53.6	54.1		
Mean	54.5	54.9		
SD	11.0	11.2		
Range	29 – 85	28 – 81		
Evidence of cancer at time of last contact			5.33	.008
Yes	17 (24.3)	6 (6.8)		
No	53 (75.7)	88 (93.6)		

a) Controls were matched to cases on type of axillary dissection
b) Controls were matched to cases on time since surgery

Table 2. Results of Univariate Conditional Regression Analyses. Limited to cases with moderate, severe, or very severe arm swelling

	Cases (n=45)	Controls (n=45)	OR	P value
Type of Axillary Dissection[a]			1.0	1.0
SLND	3 (6.7)	3 (6.7)		
ALND	42 (93.3)	42 (93.3)		
Years since surgery[b]			1.29	.583
Median	4.6	4.5		
Mean	6.7	6.6		
SD	4.9	4.6		
Range	0.5 – 22.8	0.7 – 18.3		
Current age, years			0.99	.687
Median	59.8	61.6		
Mean	61.0	62.0		
SD	12.6	12.0		
Range	39 – 95	37 - 88		
Type of surgery			1.45	.339
Mastectomy	32 (71.1)	27 (60.0)		
Lumpectomy	13 (28.9)	18 (40.0)		
Side of surgery			0.36	.048
Dominant	17 (37.8)	26 (57.8)		
Nondominant	28 (62.2)	19 (42.2)		
Reconstructive surgery			0.64	.350
Yes	10 (22.7)	14 (31.1)		
No	34 (77.3)	31 (68.9)		
Implant surgery			0.71	.565
Yes	7 (15.6)	9 (20.0)		
No	38 (84.4)	36 (80.0)		
TRAM surgery			0.60	.484
Yes	3 (6.7)	5 (11.1)		
No	42 (93.3)	40 (88.9)		
Number of nodes removed			1.02	.552
Median	14.0	14.0		
Mean	14.7	14.5		
SD	7.9	6.4		
Range	1 – 37	1 - 27		
Number of positive nodes			1.12	.119
Median	2.0	1.0		
Mean	3.5	1.8		
SD	4.1	2.7		
Range	0 – 18	0 - 11		
Nodal status			3.33	.067
Positive	32 (82.0)	27 (60.0)		
Negative	7 (17.9)	18 (40.0)		

Table 2. (Cont.)

Tumor size			1.03	.819
Median	2.5	2.0		
Mean	2.7	2.4		
SD	1.6	1.5		
Range	0.5 – 8.0	0.3 – 6.1		
Radiation Therapy			1.12	.809
Yes	31 (70.4)	31 (68.9)		
No	13 (29.5)	14 (31.1)		
Radiation to breast			0.73	.493
Yes	27 (61.4)	31 (68.9)		
No	17 (38.6)	14 (31.1)		
Radiation to axilla			9.00	.037
Yes	10 (22.7)	2 (4.4)		
No	34 (77.3)	43 (95.6)		
Radiation to supraclavicular area			0.71	.565
Yes	10 (22.7)	12 (26.7)		
No	34 (77.3)	33 (73.3)		
Chemotherapy			3.50	.118
Yes	37 (86.0)	32 (71.1)		
No	6 (13.9)	13 (28.9)		
Hormone therapy			0.61	.280
Yes	27 (61.4)	33 (73.3)		
No	17 (38.6)	12 (26.7)		
BMI			1.12	.010
Median	29.0	25.2		
Mean	31.2	26.2		
SD	8.5	5.4		
Range	21.0-62.8	18.3 – 43.0		
Diabetes			3.33	.067
Yes	12 (26.7)	5 (11.1)		
No	33 (73.3)	40 (88.9)		
Hypertension			1.67	.323
Yes	18 (40.0)	14 (31.1)		
No	27 (60.0)	31 (68.9)		
Drainage tubes			0.83	.763
Yes	37 (84.1)	39 (86.7)		
No	7 (15.9)	6 (13.3)		
Number of aspirations (continuous)			1.78	.045
None	31 (70.4)	38 (84.4)		
One	2 (4.5)	4 (8.9)		
Two	5 (11.4)	2 (4.4)		
Three	3 (6.8)	1 (2.2)		
More than three	3 (6.8)	0 (0)		

Table 2. (Cont.)

Prior medical condition limiting hand or shoulder movement			1.33	.706
Yes	4 (8.9)	3 (6.7)		
No	41 (91.1)	42 (93.3)		
Medical procedure on arm or hand on side of surgery			1.83	.232
Yes	15 (33.3)	10 (22.7)		
No	30 (66.7)	34 (77.3)		
Injury on arm or hand on side of surgery			0.67	.530
Yes	4 (8.9)	6 (13.9)		
No	41 (91.1)	37 (86.0)		
Strength training exercises			0.25	.032
Frequently/very frequently	3 (6.7)	12 (27.3)		
Never/occasionally	42 (93.3)	32 (72.7)		
Routine activities causing arm to ache			1.44	.396
Frequently/very frequently	15 (33.3)	11 (25.0)		
Never/occasionally	30 (66.7)	33 (75.0)		
Whirlpool, hot tub, or sauna use			0.25	.215
Frequently/very frequently	1 (2.3)	4 (9.1)		
Never/occasionally	43 (97.7)	40 (90.9)		
Usually lift more than 10 pounds			0.69	.396
Yes	21 (48.8)	25 (56.8)		
No	22 (51.2)	19 (43.2)		
Any air travel since breast surgery			0.35	.048
Yes	24 (54.5)	34 (75.6)		
No	20 (45.4)	11 (24.4)		
Wears breast prosthesis			1.50	.442
Yes	17 (37.8)	14 (31.1)		
No	28 (62.2)	31 (68.9)		

Table 2. (Cont.)

Ever wear compression sleeve			1.00	1.00
Yes	6 (13.3)	6 (13.3)		
No	39 (86.7)	39 (86.7)		
Smoking			8.50	.004
Ever	26 (57.8)	11 (24.4)		
Never	19 (42.2)	34 (75.6)		
Age at time of surgery			0.99	.665
Median	54.1	53.7		
Mean	54.3	55.4		
SD	11.5	11.6		
Range	30 - 85	30 - 81		
Evidence of cancer at time of last contact			5.00	.038
Yes	10 (30.3)	3 (6.7)		
No	23 (69.7)	42 (93.3)		

a) Controls were matched to cases on type of axillary dissection
b) Controls were matched to cases on time since surgery

Table 3. Patient-Identified Events Attributable to Lymphedema Development

Category	**Number of Patients**
Exercise/ride bike/golf/yoga/gardening	10
Trauma or infection to arm or hand (cuts, fracture, bug bite, sleeping on limb)	9
Lifted heavy weight	8
Medical/Surgical Procedures (BP, blood draw, port installation)	5
Treatment for breast cancer (radiation therapy - 2, chemotherapy – 3, surgery - 2)	5
Typing/repetitive motion/painting	5
Heat/humidity	4
Airplane trip	4
Sitting motionless/normal activities of daily living	4

Figure 1. Proportion of Patient Reporting Interference with Daily Activity From Arm or Hand Swelling by Amount of Swelling

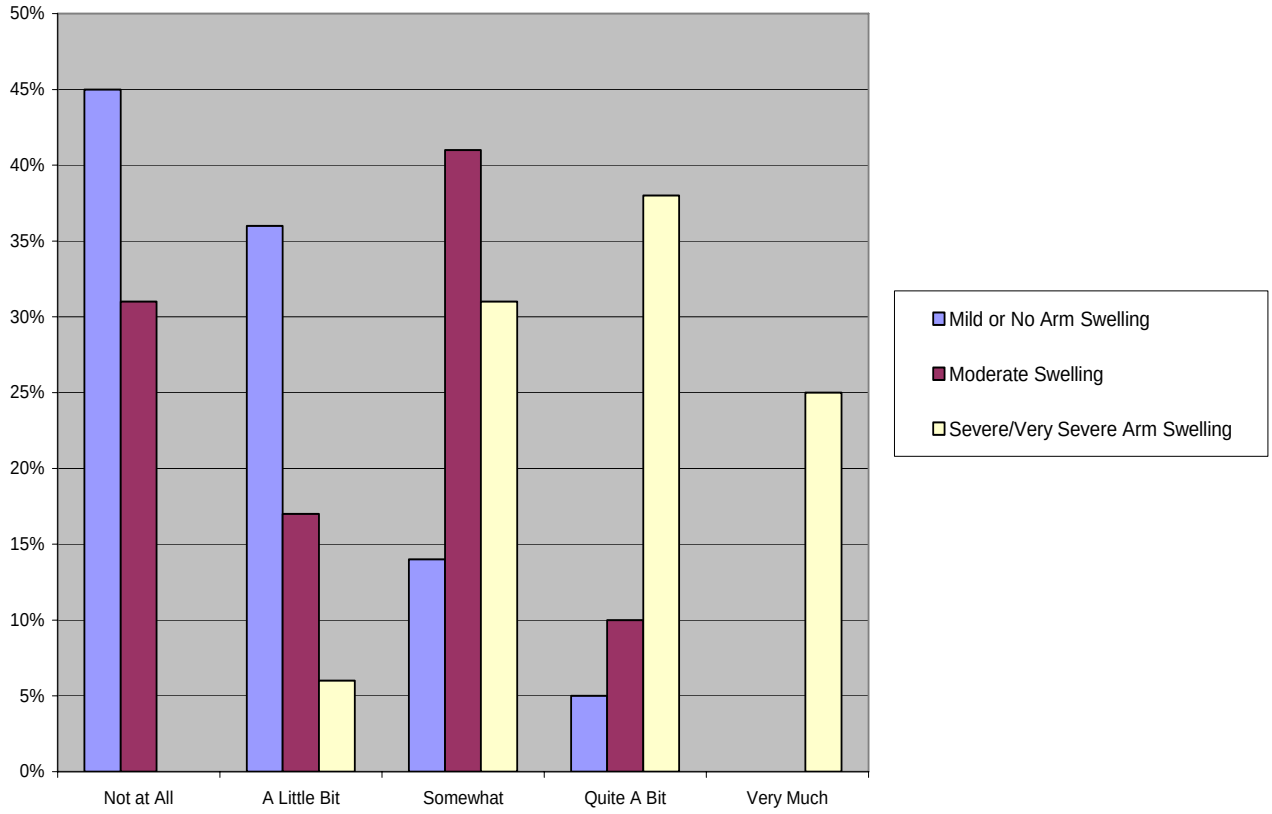

Figure 2. SF-36 Subscales and Summary Component Scales